REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Entry of this Amendment is proper under 37 C.F.R. 1.116, because the Amendment places the application in condition for allowance for the reasons discussed herein; does not introduce any new claims; does not raise any new issue requiring further search and/or consideration because the amendments amplify issues previously discussed throughout prosecution, and places the application in better form for an appeal should an appeal be necessary.

As set forth in the Office Action Summary, claims 1-17, 20, 21 and 23-30 are pending. Claims 11-17, 20, 23-25 and 27-29 stand withdrawn. Claims 1-6, 8-10 and 26 are amended herein. Claims 7, 21 and 30 are canceled herein without predjudice or disclaimer thereto. New claim 31 is added. The specification and abstract are also amended to address issues of priority and language.

Basis for the amendments and new claim may be found throughout the specification and claims as-filed, especially at page 7, lines 18-20, page 11, line 20 and page 15, lines 20-25. Thus, no new matter is set forth herein. Applicants reserve the right to file at least one continuation application to any subject matter canceled by way of the present Amendment.

Priority and Specification

The Office Action states that the specification must contain a statement regarding prior applications, for purposes of priority. Thus, the specification is

amended herein to recite the priority information as set forth in the Request for Utility Application as-filed.

The specification stands objected to as the Abstract purportedly recites "said". The Abstract is amended herein to remove legal phraseology.

Claim Objections

Claim 1 is objected to for the recitation of "all of part". Applicants note this term was a typographical error, and have amended claim 1 to recite "all or part". Claim 10 is objected to for the recitation of "gp16O". Claim 10 is amended herein to recite "gp160". In light of the above, Applicants request that the objections to the claims be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-10, 21, 26 and 30 stand rejected under 35 U.S.C. § 112, second parargraph as purportedly indefinite. Specifically, independent claim 1 stands rejected for the recitation of "a promoter and/or regulatory sequence" as it appears that claim 1 recites a nucleic acid that does not contain a promoter, but only a regulatory sequence. Applicants refer to pages 7-8 of the specification, which discuss in detail the "elements which ensure the expression of said gene *in vivo*", as referring to elements required in order to ensure the expression of the gene and its transfer into the target cell. "Promoters and/or regulatory sequences", as noted on page 8, apply to the present invention. A detailed discussion is also provided on page 8 regarding choosing and using the promoters and/or regulatory sequences in

the context of the invention, it would be clear what is meant by "promoter and/or regulatory sequence" in claim 1.

Claim 3 stands rejected for the recitation of "said target cells" as this phrase purportedly lacks antecedent basis in claim 1. Claim 3 is amended to recite "said target cell", as recited in claim 1.

In light of the above, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

Hayden et al. as evidenced by Janeway, Jr.

Claims 1-5, 7-9 , 21 and 30 stand newly rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Hayden et al. (*Tissue Antigens* 1996; 48:242-54) and as evidenced by Janeway, Jr. (*Immunobiol.* 1999).

The Office Action states that Hayden et al. disclose a retroviral vector comprising a gene that encodes heavy and light chain of a single chain antibody that recognizes CD28. The Office Action also states that the CD28 receptor consists of TCRα and TCRβ chains, as per Janeway, Jr.

Applicants traverse the rejection, and submit that the cited references fail to recite every element of the presently claimed invention as amended. To anticipate a claim, a single prior art reference must teach each and every element of the claimed invention. *See e.g.,* M.P.E.P. 2131; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

Claim 1, as amended herein, is directed to a pharmaceutical composition for treating mammals, comprising at least one nucleic acid sequence containing at least one gene of therapeutic interest, and a promoter and/or regulatory sequence which ensures the expression of said gene *in vivo* in a target cell intended to be genetically modified with said nucleic acid sequence. The gene of therapeutic interest encodes all or part of an antibody fused with a transmembrane polypeptide, and the antibody is capable of binding to a polypeptide. As recited in claim 1 herein, the polypeptide is all or part of the TCR-α, TCR-β or CD3. The pharmaceutical composition also comprises a compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes, as well as an acceptable vehicle.

In the interest of expediting prosecution and as mentioned above, the claims are amended to recite pharmaceutical compositions comprising nucleic acid sequence encoding all or part of an antibody capable of binding TCRα, TCRβ and CD3. This is discussed in the present specification on page 11. Hayden does not recite this element of the claimed invention, let alone each and every element.

Janeway is purportedly cited to show that the CD28 receptor consists of TCRα and TCRβ chains. Applicants submit this is not the case. Janeway does not disclose that CD28 consists of TCRα and TCRβ chains. Section 4-23 (also cited in the Office Action in this regard on page 5) does not mention CD28 at all, and so no information regarding CD28 can be obtained from it by the skilled artisan. Furthermore, Figures 8.10 of Janeway cited in the Office Action show that CD28 is structurally different from the TCR/CD3 complex.

Thus, Janeway, Jr. does not recite each element of the present invention either. Even though Janeway is cited as a supporting reference, as set forth in

M.P.E.P. § 2131.01, more than one reference should be cited in support of a rejection under 35 U.S.C. § 102 only if the second reference is cited to prove the primary reference contains an enabled disclosure; explain the meaning of a term used in the primary reference; or show that a characteristic not disclosed in the reference is inherent. It is unclear as to why the second reference, Janeway, Jr. is cited herein.

Regardless, Hayden fails to recite each element of the presently claimed invention. Applicants request that this rejection be withdrawn.

Ledbetter *et al.*

Claims 1-9, 21, 26 and 30 stand newly rejected under 35 U.S.C. § 102(e) as purportedly anticipated by Ledbetter et al. (U.S. Patent No. 6,699,715) as evidenced by Gilliand et al. (*Tissue Antigens* 1996;47:1-20). Ledbetter *et al.* is cited for purportedly disclosing a biological material comprising a modified single chain variant (scFv) molecule containing a binding site of an antibody and at least a portion of a transmembrane domain of a T cell receptor.

In the interest of expediting prosecution and without acquiescing in the rejection, Applicants have amended the present claims to recite pharmaceutical compositions comprising at least one nucleic acid sequence containing at least one gene of therapeutic interest and a promoter and/or regulatory sequence which ensures the expression of said gene *in vivo* in a target cell intended to be genetically modified with said nucleic acid sequence. The gene of therapeutic interest encodes all or part of an antibody fused with a transmembrane polypeptide, and this antibody is capable of binding to a polypeptide which is selected from the group consisting of

all or part of the TCRα, TCRβ, or CD3. The composition also comprises a compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes and a pharmaceutically acceptable vehicle (*see* page 15, lines 20-25 of the specification).

Ledbetter *et al.* do not disclose the claimed pharmaceutical composition, and certainly not one comprising compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes. Thus, as Ledbetter *et* al. do not recite every element of the present invention, Applicants request that this rejection be withdrawn.

Wittrup *et al.*

Claims 1-3 and 30 stand rejected under 35 U.S.C. § 102(e) as purportedly anticipated by Wittrup et al. (U.S. Patent No. 6,423,538) as evidenced by Lu et al. (*Biochim. Biophys. Acta* 2000; 1491:13-9). Wittrup et al. is cited for purportedly disclosing a DNA plasmid vector comprising a gene of interest and a Gal promoter and regulatory sequence such as f1(+) origin, wherein the gene of interest is a single chain anti-TCR antibody KJ16.

As noted above, the claims are amended herein. Wittrup et al. fails to disclose the claimed pharmaceutical composition, comprising compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes. Finally, it is unclear why Lu *et al.* is cited in this context. Applicants request that this rejection be withdrawn.

German *et al.*

Claims 1-6, 21, 26 and 30 stand rejected by the Examiner for being purportedly anticipated by German et al. (U.S. Patent No. 6,531,455).

German et al. is cited for purportedly disclosing methods for delivering a polypeptide to the bloodstream of a subject by the introduction of a nucleic acid construct into secretory gland cells (*see* the Abstract of German et al.). However, this indicates that the nucleic acid disclose by German et al. comprises a gene coding for a soluble protein. Such a gene does not comprise a region which allows the anchoring to the cell membrane as recited in the rejected claims.

The Office Action states that the rejected claims do not contain the element of comprising a membrane anchoring sequence, and therefore that German et al. recites the elements of the claims. Applicants disagree. Claim 1, even before amendments made herein, recited that the antibody would be expressed at the surface of the target cell, which clearly indicates the need of a membrane anchoring sequence. However, in the interest of expediting prosecution, claim 1 is amended herein to recite nucleic acid sequences encoding an antibody fused with a transmembrane polypeptide. German et al. does not recite each element of the present invention, let alone an antibody which is expressed at the surface of the target cell, indicating the need for a membrane anchoring sequence, as noted in the Office Action.

In light of the above, Applicants request that the rejections under 35 U.S.C. § 102 be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 1, 5, 7, 9 and 10 stand newly rejected as purportedly unpatentable over Ledbetter *et al.* in view of Allison *et al* (U.S. Patent No. 5,811,097)., Gupta *et al.*

(*DNA Cell. Biol.* 1998 Jul;17:573-81), and Antoine *et al.* (*Virol.* 1998 May;244:365-96). Applicants respectfully traverse.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. § 2142. Applicants respectfully submit that these criteria have not been met in the present Office Action.

Ledbetter et al. is cited for purportedly disclosing a biological material comprising a modified single chain variant (scFv) molecule containing a binding site of an antibody and at least a portion of a transmembrane domain of a T cell receptor. Allison *et al.* and Gupta *et al.* purportedly disclose a transmembrane polypeptide. Antoine is cited for purportedly disclosing that the MVA vector is well known in the art as a vaccine carrier and that the rabies glycoprotein could be constructed in such a recombination product.

As previously noted, Applicants have amended the present claims to recite compositions comprising a compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes, as well as for the biological material already recited in the claims as-filed.

Ledbetter *et al.* fails to disclose the claimed composition. Allison *et al.*, Gupta *et al.* and Antoine *et al.*, the secondary references, also fail to disclose the use of the biological material of Ledbetter *et al.* in combination with a compound which is naturally for the activation of cytotoxic effector cells of helper T lymphocytes. Thus, the cited references, taken in combination, fail to recite the elements of the present

invention and fail to provide a motivation to arrive at the present invention, let alone any expectation of success in this regard. The skilled artisan would not have been motivated to produce or use the presently claimed pharmaceutical compositions, based on the combined disclosure of the cited references.

Thus, Applicants request that the rejections under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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